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RDISCLOSURE on STN Easy enhanced with new search and display BIOSIS reloaded and enhanced with archival data MAY 21 TOXCENTER enhanced with BIOSIS reload NEWS 16 NEWS 17 MAY 21 CA/CAplus enhanced with additional kind codes for German patents NEWS 18 MAY 22 CA/CAplus enhanced with IPC reclassification in Japanese patents NEWS 19 JUN 27 CA/CAplus enhanced with pre-1967 CAS Registry Numbers NEWS 20 JUN 29 STN Viewer now available NEWS 21 STN Express, Version 8.2, now available JUN 29

NEWS 22 JUL 02 LEMBASE coverage updated
NEWS 23 JUL 02 LMEDLINE coverage updated

NEWS 24 JUL 02 SCISEARCH enhanced with complete author names

NEWS 25 JUL 02 CHEMCATS accession numbers revised

NEWS 26 JUL 02 CA/CAplus enhanced with utility model patents from China

NEWS EXPRESS 29 JUNE 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH, VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 05 JULY 2007.

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NEWS IPC8 For general information regarding STN implementation of IPC 8

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=> S (POLY (5A) ICLC)

706494 POLY

2 POLIES

706495 POLY

(POLY OR POLIES)

105 ICLC

L1 94 (POLY (5A) ICLC)

=> d scan

L1 94 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN

CC 1-6 (Pharmacology)

TI Cellular regulation by immunomodifiers MVE-2 and poly ICLC and their therapeutic application

ST immunomodifier antitumor cell regulation; MVE 2 antitumor immunomodifier; polymer lysine nucleotide immunomodifier antitumor

IT Lymphokines and Cytokines

RL: BIOL (Biological study)

(colony-stimulating factor secretion by, immunomodifiers effect on, neoplasm inhibition in relation to)

IT Neoplasm inhibitors

(immunomodifiers, cell regulation in relation to)

IT Immune adjuvants

IT Prostaglandins

RL: FORM (Formation, nonpreparative)

(E, formation of, immunomodifiers effect on, neoplasm inhibition in relation to)

IT Macrophage

(cytotoxic, immunomodifiers, neoplasm inhibition in relation to)

IT Lymphocyte

(natural killer, immunomodifiers, neoplasm inhibition in relation to)

IT 50-18-0

```
RL: BIOL (Biological study)
          (neoplasm inhibition by MVE-2 and, immune modulation in)
IT
      27100-68-1
                      59789-29-6
      RL: BAC (Biological activity or effector, except adverse); BSU (Biological
      study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
          (neoplasm inhibition by, immune modulation in, cellular regulation in
          relation to)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0
=> 11 and prep/rl
         4430063 PREP/RL
                2 L1 AND PREP/RL
L<sub>2</sub>
=> d 12 1-2
      ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
L2
ΑN
      2004:18891 CAPLUS
DN
      140:71067
TΤ
      Method for preparation of large volume batches of poly-
      ICLC with increased biological potency, and therapeutic, clinical
      and veterinary uses thereof
IN
      Salazar, Andres
      Oncovir, Inc., USA
PA
      U.S. Pat. Appl. Publ., 14 pp.
SO
      CODEN: USXXCO
DT
      Patent
LA
      English
FAN.CNT 1
      PATENT NO.
                                KIND
                                         DATE
                                                        APPLICATION NO.
                                         ----
      ______
                                _ _ _ _
                                                        -----
ΡI
      US 2004005998
                                 A1
                                         20040108
                                                        US 2003-611614
                                                                                      20030701
      WO 2005102278
                                 Α1
                                         20051103
                                                        WO 2003-US20828
                                                                                      20030701
                AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
                VN, YU, ZA, ZW
           RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
      AU 2003248791
                                         20051109
                                                      AU 2003-248791
                                 Α1
                                                                                      20030701
      EP 1778186
                                         20070502
                                 A1
                                                       EP 2003-819324
                                                                                      20030701
                AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PT, RO, SE, SI, SK, TR
PRAI US 2002-393713P
                                 P
                                         20020703
      WO 2003-US20828
                                 W
                                         20030701
      ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
AN
      1982:135517 CAPLUS
DN
      96:135517
ΤI
      Polyriboinosinic-polyribocytidylic acid-poly-L-lysine complex [poly(ICL)]
      without carboxymethylcellulose (CMC): a new primate-effective interferon
      inducer
      Riley, Freddie L.; Morin, Martin L.; Lvovsky, Eduard; Stephens, Edward E.;
ΑU
      Levy, Hilton B.
CS
      Natl. Inst. Allergy Infect. Dis., Bethesda, MD, 21701, USA
      Proceedings of the Society for Experimental Biology and Medicine (1982),
so
      169(2), 183-8
      CODEN: PSEBAA; ISSN: 0037-9727
DT
      Journal
LA
      English
```

Effect of treatment with exogenous interferon, polyriboinosinic-polyribocytidylic acid, or polyriboinosinic-polyribocytidylic

acid-poly-L-lysine complex on Herpesvirus hominis infections in mice interferon inducer herpesvirus infection; ribonucleotide hypervirus infection; polyriboinosinic acid polyribocytidylic acid herpesvirus;

```
polyribocytidylate polylysine polyriboinosinate herpesvirus
IT
     Interferons
     RL: BIOL (Biological study)
        (herpesvirus infection treatment with)
IT
     Virus, animal
        (Herpesvirus hominis type 2, infection with, interferon and interferon
        inducers treatment of)
IT
     24939-03-5
                  64769-70-6
     RL: BIOL (Biological study)
        (herpesvirus infection treatment with)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
L1
      94 ANSWERS
                   CAPLUS COPYRIGHT 2007 ACS on STN
CC
     1-7 (Pharmacology)
     Purification of carboxymethylcellulose decreases toxicity of poly
     ICLC in mice
ST
     polyinosinylcytidylate polylysine carboxymethylcellulose interferon
     toxicity
TT
     Interferons
     RL: PRP (Properties)
        (induction of, with polyinosinic polycytidylic acid-polylysine-
        carboxymethylcellulose, carboxymethylcellulose purification effect on,
        toxicity in relation to)
IT
     59789-29-6
     RL: PRP (Properties)
        (toxicity of, carboxymethylcellulose purification decrease of, interferon
        induction in relation to)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
      94 ANSWERS
                   CAPLUS COPYRIGHT 2007 ACS on STN
L1
CC
     15-5 (Immunochemistry)
TI
     TNF-\alpha is a principal cytokine involved in the recruitment of NK
     cells to liver parenchyma
ST
     tumor necrosis factor natural killer lymphocyte; liver NK lymphocyte tumor
     necrosis factor
IT
     Liver
        (natural killer lymphocyte adhesion to endothelium of, tumor necrosis
        factor-\alpha involvement in)
IT
        (bio-, of natural killer cells to liver endothelium, tumor necrosis
        factor-\alpha involvement in)
     Lymphocyte
IT
        (natural killer cell, adhesion of, to liver endothelium, tumor necrosis
        factor-\alpha involvement in)
IT
     Lymphokines and Cytokines
     RL: BIOL (Biological study)
        (tumor necrosis factor-\alpha, in natural killer cell adhesion to
        liver endothelium)
IT
     24939-03-5, Polyinosinic-polycytidylic acid
                                                    25104-18-1, Poly-L-lysine
     RL: BIOL (Biological study)
        (hepatic natural killer lymphocyte activity enhancement by)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
L1
      94 ANSWERS
                   CAPLUS COPYRIGHT 2007 ACS on STN
CC
     15-13 (Immunochemistry)
     Section cross-reference(s): 1
TT
     Adjuvant effects of low doses of a nuclease-resistant derivative of
     polyinosinic acid.polycytidylic acid on antibody responses of monkeys to
     inactivated Venezuelan equine encephalomyelitis virus vaccine
     immune adjuvant polyinosinate polycytidylate; polylysine polyIC immune
ST
     adjuvant; CM cellulose polyIC immune adjuvant
IT
     Immune adjuvants
```

```
(polyinosinic acid polycytidylic acid-polylysine-
        carboxymethylcellulose complexes as, at low doses)
IT
     59789-29-6
     RL: BIOL (Biological study)
        (immune adjuvanticity of, at low doses)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
      94 ANSWERS
L1
                   CAPLUS COPYRIGHT 2007 ACS on STN
CC
     1-6 (Pharmacology)
TI
     Immunotherapy of metastasis: comparative efficacy of BRMs for the
     treatment of transplantable and autochthonous tumors
ST
     biol response modifier antimetastatic; immunomodulator antimetastatic
     Immune adjuvants
TT
        (neoplasm metastasis treatment with)
IT
     Neoplasm inhibitors
        (metastasis, immunomodulating agents as)
TT
     27100-68-1
                  37339-90-5
                               39325-01-4
                                           59789-29-6
                                                          79335-75-4
     RL: BIOL (Biological study)
        (neoplasm metastasis treatment with, immunomodulating activity in)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
L1
      94 ANSWERS
                   CAPLUS COPYRIGHT 2007 ACS on STN
CC
     1-5 (Pharmacology)
     Killing of Leishmania donovani amastigotes by poly ICLC
ΤI
     in hamsters
ST
     Leishmania amastigote antileishmanial polyinosinate polycytidylate
     arginine
IT
     Leishmania donovani
        (killing of Leishmania donovani amastigotes by poly
        ICLC and L-arginine in hamsters)
IT
     Microbicidal and microbiostatic action
        (leishmanicidal, killing of Leishmania donovani amastigotes by
        poly ICLC and L-arginine in hamsters)
IT
     10102-43-9, Nitric oxide, biological studies 125978-95-2, Nitric oxide
     synthase
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (in killing of Leishmania donovani amastigotes by poly
        ICLC and L-arginine in hamsters)
IT
     74-79-3, L-Arginine, biological studies
                                               59789-29-6, Poly
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (killing of Leishmania donovani amastigotes by poly
        ICLC and L-arginine in hamsters)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
L1
      94 ANSWERS
                   CAPLUS COPYRIGHT 2007 ACS on STN
     15-13 (Immunochemistry)
CC
     Section cross-reference(s): 1
TI
     Immune modulating effects of poly ICLC
     immune adjuvant interferon inducer; polynucleotide polylysine complex
ST
     immune adjuvant
IT
     Immune adjuvants
        ((poly I poly C) polylysine-carboxymethylcellulose complexes as,
        interferon induction in relation to)
IT
     Vaccines
        (immune adjuvant activity of interferon inducers with)
     Interferons
IŢ
     RL: PRP (Properties)
       (induction of, with (poly I poly C) -polylysine-
```

```
carboxymethylcellulose complexes, immune adjuvant activity in relation
        to)
     59789-29-6
IT
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (immune adjuvant activity of, interferon induction in relation to)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
      94 ANSWERS
L1
                   CAPLUS COPYRIGHT 2007 ACS on STN
CC
     1-6 (Pharmacology)
ΤI
     Toxicity of polyinosinic-polycytidylic acid admixed with poly-L-lysine and
     solubilized with carboxymethylcellulose in mice
ST
     poly ICLC toxicity; polyinosinate polycytidylate
     polylysine toxicity
IT
     Liver, toxic chemical and physical damage
     Lung, toxic chemical and physical damage
        (polyinosinate-polycytidylate-polylysine toxicity to)
IT
     59789-29-6, Poly (ICLC)
     RL: PRP (Properties)
        (toxicity of, to liver and lungs)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
Ll
      94 ANSWERS
                   CAPLUS COPYRIGHT 2007 ACS on STN
TТ
     Immunochemotherapy for Leishmania donovani infection in golden hamsters:
     combinatorial action of poly ICLC plus L-arginine and
     sodium stibogluconate (Stibanate)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
L1
      94 ANSWERS
                   CAPLUS COPYRIGHT 2007 ACS on STN
CC
     1-7 (Pharmacology)
     Section cross-reference(s): 15
     Interferon induction and therapy of brain tumors in rats by poly
ΤI
     (ICLC)
     polyriboinosinate polyribocytidylate analog interferon antitumor; brain
ST
     tumor polyriboinosinate polyribocytidylate analog; polylysine CM cellulose
     polynucleotide interferon induction
IT
     Interferons
     RL: PRP (Properties)
        (induction of, by poly(I) poly(C) -polylysine-CM cellulose, in
        brain tumor immunotherapy)
IT
     Immune adjuvants
        (interferon induction and brain tumor inhibition by
        poly(I) · poly(C) -polylysine-CM cellulose in relation to)
TΤ
     Brain, neoplasm
        (interferon induction by poly(I) poly(C) polylysine-CM cellulose
        in immunotherapy of)
TΤ
     Neoplasm inhibitors
        (poly(I) poly(C) polylysine-CM cellulose as, for brain neoplasm,
        interferon induction in relation to)
IT
     59789-29-6
     RL: BIOL (Biological study)
        (interferon induction and brain tumor inhibition by)
TT
     24939-03-5
     RL: BIOL (Biological study)
        (interferon induction and brain tumor inhibition by analog of)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
1.1
      94 ANSWERS
                   CAPLUS COPYRIGHT 2007 ACS on STN
CC
     15-5 (Immunochemistry)
     Section cross-reference(s): 1
     Activation of natural killer cells in newborn piglets by interferon
```

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induction
     natural killer cell interferon activation; piglet immunity interferon
ST
     inducer
IT
     Interferons
     RL: PRP (Properties)
        (natural killer cell activation by exogenous and induction of, in
IT
        (natural killer lymphocyte activation in newborn and weanling,
        interferon induction of)
IT
     Lymphocyte
        (natural killer, activation of, by interferon, in piglets)
IT
     Virus, animal
        (transmissible gastroenteritis, infection with, in piglets, interferon
        induction inhibition of)
IT
     59789-29-6, Poly ICLC
     RL: BIOL (Biological study)
        (interferon induction by, natural killer cell response to, in piglets)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
L1
      94 ANSWERS
                   CAPLUS COPYRIGHT 2007 ACS on STN
IC
     ICM A61K038-16
     ICS A61K031-716
INCL 514002000; 514057000
     1-12 (Pharmacology)
     Method for preparation of large volume batches of poly-
ΤI
     ICLC with increased biological potency, and therapeutic, clinical
     and veterinary uses thereof
ST
     poly ICLC prodn therapeutic gene regulation; infection
IT
     CD antiqens
     RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD106; preparation of large volume batches of poly-ICLC
        with increased biol. potency, and therapeutic use)
     Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
IT
        (DNA helicase; preparation of large volume batches of poly-
        ICLC with increased biol. potency, and therapeutic use)
IT
     Nervous system, disease
        (Guillain-Barre syndrome; preparation of large volume batches of poly
        -ICLC with increased biol. potency, and therapeutic use)
IT
     Enzymes, biological studies
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (RNA helicase; preparation of large volume batches of poly-
        ICLC with increased biol. potency, and therapeutic use)
IT
     Infection
     Respiratory system, disease
        (SARS (severe acute respiratory syndrome); preparation of large volume
        of poly-ICLC with increased biol. potency, and
        therapeutic use)
     Cell adhesion molecules
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (VCAM-1 (vascular cell adhesion mol. 1); preparation of large volume batches
        of poly-ICLC with increased biol. potency, and
        therapeutic use)
     Proteins
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (actin filament-associated; preparation of large volume batches of poly
        -ICLC with increased biol. potency, and therapeutic use)
IT
     Neuroglia, neoplasm
        (astrocytoma; preparation of large volume batches of poly-
        ICLC with increased biol. potency, and therapeutic use)
IT
     Respiratory system, disease
        (bovine respiratory complex; preparation of large volume batches of
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poly-ICLC with increased biol. potency, and
        therapeutic use)
IT
    Intestine, neoplasm
        (colon; preparation of large volume batches of poly-ICLC
        with increased biol. potency, and therapeutic use)
IT
     Enzymes, biological studies
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (dsRNA-inducible; preparation of large volume batches of poly-
        ICLC with increased biol. potency, and therapeutic use)
IT
     Translation initiation factors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (eIF-2; preparation of large volume batches of poly-ICLC
        with increased biol. potency, and therapeutic use)
TT
     Encephalitis
        (equine viral; preparation of large volume batches of poly-
        ICLC with increased biol. potency, and therapeutic use)
IT
     Neuroglia, neoplasm
        (glioblastoma; preparation of large volume batches of poly-
        ICLC with increased biol. potency, and therapeutic use)
IT
     Immune disease
        (immune neuropathy; preparation of large volume batches of poly-
        ICLC with increased biol. potency, and therapeutic use)
IT
     Interferons
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (induction; preparation of large volume batches of poly-ICLC)
        with increased biol. potency, and therapeutic use)
IT
     Drug delivery systems
        (injections, i.m.; preparation of large volume batches of poly-
        ICLC with increased biol. potency, and therapeutic use)
TT
     Drug delivery systems
        (injections, i.v.; preparation of large volume batches of poly-
        ICLC with increased biol. potency, and therapeutic use)
IT
     Ionizing radiation
        (injury; preparation of large volume batches of poly-ICLC.
        with increased biol. potency, and therapeutic use)
TT
     Transcription factors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (interferon regulatory factor; preparation of large volume batches of
        poly-ICLC with increased biol. potency, and
        therapeutic use)
IT
     Infection
        (microbial; preparation of large volume batches of poly-ICLC
        with increased biol. potency, and therapeutic use)
IT
     Drug delivery systems
        (nasal; preparation of large volume batches of poly-ICLC
        with increased biol. potency, and therapeutic use)
TT
     Astrocyte
        (neoplasm, astrocytoma; preparation of large volume batches of poly-
        ICLC with increased biol. potency, and therapeutic use)
IT
     Nerve, disease
        (neuropathy, immune; preparation of large volume batches of poly-
        ICLC with increased biol. potency, and therapeutic use)
IT
     Drug delivery systems
        (oral; preparation of large volume batches of poly-ICLC
        with increased biol. potency, and therapeutic use)
IT
     Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (p56; preparation of large volume batches of poly-ICLC
        with increased biol. potency, and therapeutic use)
TТ
     AIDS (disease)
     Adenoviridae
     Anti-AIDS agents
     Anti-infective agents
     Antitumor agents
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Antiviral agents

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Apoptosis
Biological transport
Brain, neoplasm
Cell cycle
Coronavirus
Cytoskeleton
Dengue virus
Drug delivery systems
Ebola virus
Extracellular matrix
Filovirus
Flavivirus
Foot-and-mouth disease virus
Hepatitis virus
Herpesviridae
Human
Human adenovirus
Human herpesvirus
Human immunodeficiency virus
Immunostimulants
Influenza virus
Japanese encephalitis virus
Leukemia
Lung, neoplasm
Lymphoma
Mammary gland, neoplasm
Melanoma
Metabolism
Multiple sclerosis
Neuroglia, neoplasm
Porcine respiratory and reproductive syndrome virus
Poxviridae
RNA formation
Radioprotectants
Sarcoma
Signal transduction, biological
Translation, genetic
Vaccines
Vaccinia virus
Variola virus
West Nile virus
Yellow fever virus
   (preparation of large volume batches of poly-ICLC with
   increased biol. potency, and therapeutic use)
Cytokines
Double stranded RNA
Gene, animal
Growth factors, animal
Tumor necrosis factors
p53 (protein)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
   (preparation of large volume batches of poly-ICLC with
   increased biol. potency, and therapeutic use)
Kidney, neoplasm
   (renal cell carcinoma; preparation of large volume batches of poly-
   ICLC with increased biol. potency, and therapeutic use)
Carcinoma
   (renal cell; preparation of large volume batches of poly-
   ICLC with increased biol. potency, and therapeutic use)
Drug delivery systems
   (sublingual; preparation of large volume batches of poly-
   ICLC with increased biol. potency, and therapeutic use)
Drug delivery systems
   (topical; preparation of large volume batches of poly-ICLC
   with increased biol. potency, and therapeutic use)
```

IT

IT

IT

IT

IT Drug delivery systems (transdermal; preparation of large volume batches of poly-ICLC with increased biol. potency, and therapeutic use) TT (vaccine; preparation of large volume batches of poly-ICLC with increased biol. potency, and therapeutic use) IT Blood vessel, disease (vasculitides; preparation of large volume batches of poly-ICLC with increased biol. potency, and therapeutic use) (viral; preparation of large volume batches of poly-ICLC with increased biol. potency, and therapeutic use) 62031-54-3, Fibroblast growth factor IT 69106-44-1, 2',5'-Oligoadenylate 91608-96-7, p68 Protein kinase synthetase 105913-11-9, Plasminogen 141907-41-7, Matrix metalloproteinase activator RL: BSU (Biological study, unclassified); BIOL (Biological study) (preparation of large volume batches of poly-ICLC with increased biol. potency, and therapeutic use) 59789-29-6P, Poly-ICLC IT RL: IMF (Industrial manufacture); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of large volume batches of poly-ICLC with increased biol. potency, and therapeutic use) IT 9004-32-4, Carboxymethyl cellulose sodium salt 25104-18-1, Poly-L-lysine 30811-80-4, Poly C 30918-54-8, Polyinosinic acid 38000-06-5, Poly-L-lysine RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of large volume batches of poly-ICLC with increased biol. potency, and therapeutic use) HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1 CAPLUS COPYRIGHT 2007 ACS on STN L194 ANSWERS CC 2-9 (Mammalian Hormones) Section cross-reference(s): 15 TI Prostaglandin E synthesis and release by murine macrophages and human monocytes after in vitro treatment with biological response modifiers prostaglandin macrophage monocyte biol modifier; lipopolysaccharide prostaglandin macrophage monocyte; polynucleotide complex prostaglandin macrophage monocyte IT Macrophage (PGE formation by, biol. response modifiers effect on) ΙT Monocyte (PGE formation by, biol. response modifiers effect on human) Lipopolysaccharides RL: BIOL (Biological study) (PGE formation response to, in macrophage and monocyte of human and laboratory animal) IT Prostaglandins RL: FORM (Formation, nonpreparative) (E, formation of, by macrophage and monocyte, of human and laboratory animal, biol. response modifiers effect on) IT Interferons $(\alpha$ -, PGE formation response to, in macrophage and monocyte of human and laboratory animal) Interferons IT(β-, PGE formation response to, in macrophage and monocyte ofhuman and laboratory animal) IT 27100-68-1 64118-86-1 64769-70-6 75985-31-8 RL: BIOL (Biological study) (PGE formation response to, in macrophage and monocyte of human and laboratory animal)

```
CAPLUS COPYRIGHT 2007 ACS on STN
L1
      94 ANSWERS
CC
     15-5 (Immunochemistry)
     Section cross-reference(s): 1
ΤI
     Production of interferon-α induced by dsRNA in human peripheral
     blood mononuclear cell cultures: role of priming by dsRNA-induced
     interferons-\gamma and -\beta
ST
     interferon induction doublestranded RNA priming
     Ribonucleic acids
     RL: BIOL (Biological study)
        (double-stranded, interferon-α induction by, in human mononuclear
IT
     Lymphocyte
     Monocyte
        (interaction of, in interferon-\alpha induction)
TΨ
     Leukocyte
        (mononuclear, interferon-\alpha induction in human, interferon-\beta
        and -\gamma and cell-cell interactions in)
IT
     Interferons
     RL: PRP (Properties)
        (\alpha, induction of, by double-stranded RNA, in human mononuclear
        cells, priming by \gamma- and \beta-interferons in)
IT
     Interferons
     RL: BIOL (Biological study)
        (\beta, priming by, in \alpha-interferon induction by double-stranded
        RNA)
     Interferons
IT
     RL: BIOL (Biological study)
         (\gamma, \text{ priming by, in } \alpha\text{-interferon induction by}
        double-stranded RNA)
IT
     24939-03-5, Poly(I):poly(C)
                                    38640-92-5
                                                  59789-29-6, Poly(
     ICLC)
     RL: BIOL (Biological study)
         (interferon-\alpha induction by, in human mononuclear cells)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
      94 ANSWERS
                    CAPLUS COPYRIGHT 2007 ACS on STN
     15-2 (Immunochemistry)
CC
     Toll like receptor-3 ligand poly-ICLC promotes the
     efficacy of peripheral vaccinations with tumor antigen-derived peptide
     epitopes in murine CNS tumor models
ST
     TLR3 receptor ligand polyICLC CNS tumor vaccine peptide epitope
IT
     Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
         (EphA2, epitope 671-679; TLR3 receptor ligand poly-
        ICLC promotes efficacy of peripheral vaccination with tumor
        antigen-derived peptide epitopes in murine CNS tumor model)
TТ
     Toll-like receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (TLR-3; TLR3 receptor ligand poly-ICLC promotes
        efficacy of peripheral vaccination with tumor antigen-derived peptide
        epitopes in murine CNS tumor model)
     Central nervous system, neoplasm
IT
     Epitopes
     Neuroglia, neoplasm
        (TLR3 receptor ligand poly-ICLC promotes efficacy
        of peripheral vaccination with tumor antigen-derived peptide epitopes
        in murine CNS tumor model)
IT
     Peptides, biological studies
     Tumor antigens
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (TLR3 receptor ligand poly-ICLC promotes efficacy
        of peripheral vaccination with tumor antigen-derived peptide epitopes
```

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in murine CNS tumor model)
IT
     Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (TRP-2 (tyrosinase-related protein 2), epitope 180-188; TLR3 receptor
        ligand poly-ICLC promotes efficacy of peripheral
        vaccination with tumor antigen-derived peptide epitopes in murine CNS
        tumor model)
IT
     Peptides, biological studies
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (compds.; TLR3 receptor ligand poly-ICLC promotes
        efficacy of peripheral vaccination with tumor antigen-derived peptide
        epitopes in murine CNS tumor model)
TT
     T cell (lymphocyte)
        (cytotoxic; TLR3 receptor ligand poly-ICLC promotes
        efficacy of peripheral vaccination with tumor antigen-derived peptide
        epitopes in murine CNS tumor model)
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (gp100, epitope 25-33; TLR3 receptor ligand poly-ICLC
        promotes efficacy of peripheral vaccination with tumor antigen-derived
        peptide epitopes in murine CNS tumor model)
TT
     Vaccines
        (tumor; TLR3 receptor ligand poly-ICLC promotes
        efficacy of peripheral vaccination with tumor antigen-derived peptide
        epitopes in murine CNS tumor model)
IT
     Antitumor agents
        (vaccines; TLR3 receptor ligand poly-ICLC promotes
        efficacy of peripheral vaccination with tumor antigen-derived peptide
        epitopes in murine CNS tumor model)
IT
     Integrins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
                                      poly-ICLC
        (α4β1; TLR3 receptor ligand
        promotes efficacy of peripheral vaccination with tumor antigen-derived
        peptide epitopes in murine CNS tumor model)
IT
     Interferons
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (\gamma; TLR3 receptor ligand poly-ICLC promotes
        efficacy of peripheral vaccination with tumor antigen-derived peptide
        epitopes in murine CNS tumor model)
                             212370-40-6
IT
     59789-29-6, Poly-ICLC
                                            219312-69-3
     841264-18-4
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (TLR3 receptor ligand poly-ICLC promotes efficacy
        of peripheral vaccination with tumor antigen-derived peptide epitopes
        in murine CNS tumor model)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
L1
      94 ANSWERS
                   CAPLUS COPYRIGHT 2007 ACS on STN
     1-7 (Pharmacology)
CC
TI
     Poly ICLC induces anti-IC antibodies in mice and
     rabbits
ST
     poly ICLC polyinosinate polycytidylate antibody
IT
     Antibodies
     RL: BIOL (Biological study)
        (to polyinosinate · polycytidylate, poly ICLC
        induction of)
     59789-29-6
IT
     RL: BIOL (Biological study)
        (antibodies to polyinosinate polycytidylate production from)
     24939-03-5
IT
     RL: BIOL (Biological study)
        (antibodies to, poly ICLC induction of)
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HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
L1
      94 ANSWERS
                    CAPLUS COPYRIGHT 2007 ACS on STN
CC
     1-6 (Pharmacology)
TI
     Drug sensitivity tests against malignant gliomas
ST
     antitumor sensitivity test brain glioma
IT
     Brain, neoplasm
        (drug sensitivity tests against)
IT
     Transplant and Transplantation, animal
        (of glioma, antitumor drug sensitivity test using)
IT
     Radiotherapy
        (of gliomas, drug sensitivity tests for)
IT
     Neoplasm inhibitors
        (glioma, drug sensitivity tests for)
IT
     Neuroglia
        (neoplasm, drug sensitivity tests against)
TΤ
     Lymphokines and Cytokines
     RL: BIOL (Biological study)
        (tumor necrosis factor, glioma inhibition by, drug sensitivity tests
        for)
IT
     Interferons
     RL: BIOL (Biological study)
        (\alpha, glioma inhibition by, drug sensitivity tests for)
ТТ
     Interferons
     RL: BIOL (Biological study)
        (\beta, glioma inhibition by, drug sensitivity tests for)
IT
     Interferons
     RL: BIOL (Biological study)
         (\gamma, glioma inhibition by, drug sensitivity tests for)
     50-07-7, Mitomycin C 50-18-0, Cyclophosphamide 57-22-7, Vincristine 11056-06-7, Bleomycin 15663-27-1, Cisplatin 23214-92-8, Adriamycin
IT
                                                         57-22-7, Vincristine
     41598-07-6, Prostaglandin D2
                                      55661-38-6, ACNU
                                                          59789-29-6, Poly
     RL: BIOL (Biological study)
        (glioma inhibition by, drug sensitivity tests for)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
L1
      94 ANSWERS
                   CAPLUS COPYRIGHT 2007 ACS on STN
CC
     1-5 (Pharmacodynamics)
     Section cross-reference(s): 15
ΤI
     Effect of a nuclease-resistant derivative of polyriboinosinic-
     polyribocytidylic acid complex on yellow fever in rhesus monkeys (Macaca
     mulatta)
ST
     nucleotide complex virucide yellow fever; interferon yellow fever virus
IT
     Interferons
     RL: PRP (Properties)
         (induction of, by nucleotide complex, in yellow fever)
IT
     Virucides and Virustats
        (nucleotide complex)
IT
     Yellow fever
        (nucleotide complex in treatment of)
IT
     59789-29-6
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (virucidal activity of, in yellow fever)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
L1
      94 ANSWERS
                    CAPLUS COPYRIGHT 2007 ACS on STN
CC
     15-5 (Immunochemistry)
TI
     The in vitro induction of colony-stimulating factor, prostaglandin E, and
     interferon in macrophages and tumor cells by biological response modifiers
```

colony stimulating factor macrophage tumor cell; prostaglandin E

ST

macrophage tumor cell; interferon macrophage tumor cell; macrophage colony factor prostaglandin interferon; tumor cell colony factor prostaglandin interferon; biol response modifier macrophage tumor cell IT Neoplasm, metabolism (colony-stimulating factor and interferon and prostaglandin E induction in cells of, by biol. response modifiers) IT Lipopolysaccharides RL: BIOL (Biological study) (colony-stimulating factor and interferon and prostaglandin E induction in macrophage and tumor cells by) ITMacrophage (colony-stimulating factor and interferon and prostaglandin E induction in, by biol. response modifiers) TT Interferons RL: PRP (Properties) (induction of, in macrophage and tumor cells, by biol. response modifiers) IT Prostaglandins RL: PRP (Properties) (E, induction of, in macrophage and tumor cells, by biol. response modifiers) 147-84-2, biological studies IT 27100-68-1 64118-86-1 RL: BIOL (Biological study) (colony-stimulating factor and interferon and prostaglandin E induction in macrophage and tumor cells by) IT 59789-29-6 RL: BIOL (Biological study) (colony-stimulating factor in and interferon and prostaglandin E induction in macrophage and tumor cells by) IT 62683-29-8 RL: PRP (Properties) (induction of, in macrophage and tumor cells, by biol. response modifiers) HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1 94 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN 1-5 (Pharmacology) CC Section cross-reference(s): 15 Characterization of murine Caraparu Bunyavirus liver infection and immunomodulator-mediated antiviral protection sthepatitis Caraparu virus treatment immunomodulator; ribavirin interferon hepatitis Caraparu virus ΙT Immunostimulants (hepatitis from Caraparu virus response to) TT Virucides and Virustats (immunostimulants as, against Caraparu virus-induced hepatitis) Drug interactions (of γ -interferons and ribavirin, in hepatitis from Caraparu virus treatment) IT Virus, animal (caraparu, hepatitis from, immunostimulants treatment of) IT Virus, animal (hepatitis, from Caraparu, immunostimulants treatment of) IT Interferons RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) $(\alpha, \text{ hepatitis from Caraparu virus response to})$ IT Interferons RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (β, hepatitis from Caraparu virus response to) IT Interferons RL: BIOL (Biological study)

(γ, hepatitis from Caraparu virus inhibition by, ribavirin

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enhancement of)
ΙT
     6307-35-3 27100-68-1 38640-92-5, Ampligen
                                                      59789-29-6, Poly
     ICLC
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (hepatitis from Caraparu virus response to)
IT
     36791-04-5, Ribavirin
     RL: BIOL (Biological study)
        (hepatitis from Caraparu virus treatment with, \gamma-interferon
        enhancement of)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
L1
      94 ANSWERS
                   CAPLUS COPYRIGHT 2007 ACS on STN
     1-5 (Pharmacodynamics)
CC
     Section cross-reference(s): 8
     Evaluation of a nuclease-resistant derivative of poly(I).
тT
     poly(C) [poly(ICLC)] as a radioprotective
     radioprotectant ribonucleic acid complex; polyinosinic polycytidylic
ST
     complex radioprotectant
IT
     Radioprotectants
        (polyinosinic acid-polycytidylic acid complex with polylysine and
        carboxy Me cellulose)
IT
     59789-29-6
     RL: BIOL (Biological study)
        (radioprotectant)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
Ll
      94 ANSWERS
                   CAPLUS COPYRIGHT 2007 ACS on STN
CC
     1-6 (Pharmacology)
     Section cross-reference(s): 15
     Biological response modifiers: regulators of the cellular immune system
     and adjuvants in antitumor therapy
ST
     immunomodulator effector cell response antitumor
IT
     Interferons
     RL: BIOL (Biological study)
        (cell-mediated immunity response to, and neoplasm inhibition by)
IT
     Immune adjuvants
        (cell-mediated, neoplasm inhibition by)
     Neoplasm inhibitors
        (immune adjuvants, cell-mediated immunity in)
IT
     Hematopoiesis
     Macrophage
        (neoplasm-inhibiting immune adjuvants effect on)
IT
     Lymphocyte
        (natural killer, neoplasm-inhibiting immune adjuvants effect on)
IT
     27100-68-1
                  39325-01-4
                               59789-29-6
                                            75985-31-8
     RL: BIOL (Biological study)
        (cell-mediated immunity response to, and neoplasm inhibition by)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
L1
      94 ANSWERS
                   CAPLUS COPYRIGHT 2007 ACS on STN
CC
     1-5 (Pharmacology)
ΤI
     Antiviral and immunomodulating inhibitors of experimentally-induced Punta
     Toro virus infections
     Punto Toro virus virucide immunomodulator
IT
     Immunomodulators
     Virucides and Virustats
        (antiviral and immunomodulating inhibitors of exptl.-induced Punta Toro
        virus infections)
IT
     Polysaccharides, biological studies
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
```

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study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (glucomannon; antiviral and immunomodulating inhibitors of
        exptl.-induced Punta Toro virus infections)
IT
        (Punta Toro, antiviral and immunomodulating inhibitors of
        exptl.-induced Punta Toro virus infections)
IT
     Interferons
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
        (\alpha, A/D); antiviral and immunomodulating inhibitors of
       exptl.-induced Punta Toro virus infections)
IT
     54-25-1, 6-Azauridine 62-53-3, Benzenamine, biological studies
     66-81-9, Actidione 145-63-1, Suramin 471-53-4, Glycyrrhetic acid
     734-22-5, CL 259763
                         3930-19-6, Streptonigrin
                                                     4016-63-1,
     8-Bromoguanosine 6742-12-7, Formycin 12758-40-6, GE132
     19622-83-4, 7-Deoxynarciclasine 25451-90-5
                                                    27089-56-1
                                                                 27100-68-1,
             29477-83-6, Narciclasine
                                       29725-42-6
                                                   30868-30-5, Pyrazofurin
     36703-88-5, Isoprinosine
                               36791-04-5, Ribavirin 38640-92-5, Ampligen
     41729-52-6, 3-Deazaguanine
                                  42400-25-9
                                               56039-11-3, 3-Deazaguanosine
     56741-95-8, Bropirimine
                             58151-87-4
                                           59643-91-3, Imexon 59789-29-6,
                  60084-10-8, Tiazofurin
     Poly(ICLC)
                                           61367-58-6
     63166-73-4, Phyllanthoside
                                  68652-43-7, Mannozym
                                                         72161-05-8, Ribavirin
     2',3',5'-triacetate
                          72301-79-2, Enviroxime 81541-26-6, CL 246738
     82372-67-6, Pseudolycorine hydrochloride 83161-83-5,
                                   83705-13-9, Selenazofurin
     Tiazofurin-5'-monophosphate
                                                               87139-86-4, AM 3
                               96203-70-2, Pancratistatin
     87745-28-6, Bryostatin 2
                                                             99258-56-7,
                               119567-79-2, Ribamidine
     Oxamisole
                104942-51-0
                                                        122970-40-5,
                                          150316-23-7, Neurotropin
     7-Thia-8-oxoguanosine
                            141776-53-6
     159192-47-9
                  159192-48-0
                                159192-49-1
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (antiviral and immunomodulating inhibitors of exptl.-induced Punta Toro
       virus infections)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
L1
      94 ANSWERS
                  CAPLUS COPYRIGHT 2007 ACS on STN
CC
     1-5 (Pharmacodynamics)
     Section cross-reference(s): 15
ΤI
    Modified polyriboinosinic-polyribocytidylic acid complex: induction of
     serum interferon, fever, and hypotension in rabbits
ST
     polyinosinate polycytidylate polylysine complex pharmacol; interferon
     polyinosinate polycytidylate polylysine; fever polyinosinate
    polycytidylate polylysine; hypotension polyinosinate polycytidylate
    polylysine
IT
     Fever and Hyperthermia
     Hypotension
        (from poly(I)-poly(C)-poly(L-lysine) complex, interferon induction in
        relation to)
IT
     Interferons
    RL: BIOL (Biological study)
        (induction by, poly(I)-poly(C)-poly(L-lysine) complex, fever and
       hypotension in relation to)
     24939-03-5D, poly-L-lysine complex 25104-18-1D, poly(I)-poly(C) complex
     38000-06-5D, poly(I)-poly(C) complex
     RL: BIOL (Biological study)
        (fever and hypotension and interferon induction by)
IT
     50-23-7
     RL: BIOL (Biological study)
        (fever and hypotension from poly(I)-poly(C)-poly(L-lysine) complex
        decrease by, interferon induction in relation to)
```

```
Ll
      94 ANSWERS
                   CAPLUS COPYRIGHT 2007 ACS on STN
CC
     1-5 (Pharmacology)
TI
     Enhanced therapeutic efficacy of poly(ICLC) and
     ribavirin combinations against Rift Valley fever virus infection in mice
     virus infection polyICLC ribavirin
ΙT
     Virus, animal
        (Rift Valley fever, infection with, therapeutic efficacy of
        poly(ICLC) and ribavirin combinations against)
IT
     36791-04-5, Ribavirin
     RL: BIOL (Biological study)
        (Rift Valley fever virus infection response to poly(
        ICLC) and)
IT
     59789-29-6, Poly ICLC
     RL: BIOL (Biological study)
        (Rift Valley fever virus infection treatment with ribavirin and)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0
=> d his
     (FILE 'HOME' ENTERED AT 18:43:07 ON 11 JUL 2007)
     FILE 'CAPLUS' ENTERED AT 18:43:17 ON 11 JUL 2007
             94 S (POLY (5A) ICLC)
L1
L2
              2 L1 AND PREP/RL
=> s l1 and lysine and (carboxymethylcellulose OR "Carboxymethyl cellulose")
        108942 LYSINE
          2345 LYSINES
        109676 LYSINE
                 (LYSINE OR LYSINES)
          7316 CARBOXYMETHYLCELLULOSE
            62 CARBOXYMETHYLCELLULOSES
          7344 CARBOXYMETHYLCELLULOSE
                 (CARBOXYMETHYLCELLULOSE OR CARBOXYMETHYLCELLULOSES)
         37332 "CARBOXYMETHYL"
             3 "CARBOXYMETHYLS"
         37332 "CARBOXYMETHYL"
                 ("CARBOXYMETHYL" OR "CARBOXYMETHYLS")
        355188 "CELLULOSE"
          4389 "CELLULOSES"
        355685 "CELLULOSE"
                 ("CELLULOSE" OR "CELLULOSES")
         13275 "CARBOXYMETHYL CELLULOSE"
                 ("CARBOXYMETHYL" (W) "CELLULOSE")
L3
            25 L1 AND LYSINE AND (CARBOXYMETHYLCELLULOSE OR "CARBOXYMETHYL
               CELLULOSE")
=> d 13 1-25 ibib abs
     ANSWER 1 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:18891 CAPLUS
DOCUMENT NUMBER:
                         140:71067
TITLE:
                         Method for preparation of large volume batches of
                         poly-ICLC with increased biological
                         potency, and therapeutic, clinical and veterinary uses
                         thereof
INVENTOR (S):
                         Salazar, Andres
PATENT ASSIGNEE(S):
                        Oncovir, Inc., USA
SOURCE:
                         U.S. Pat. Appl. Publ., 14 pp.
                         CODEN: USXXCO
DOCUMENT TYPE:
                         Patent
```

English

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

LANGUAGE:

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
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                                -----
     US 2004005998
                         A1
                                20040108
                                            US 2003-611614
                                                                   20030701
     WO 2005102278
                         A1
                                20051103
                                            WO 2003-US20828
                                                                   20030701
             AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
             RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
             VN, YU, ZA, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2003248791
                                20051109
                                           AU 2003-248791
                          A1
                                                                   20030701
     EP 1778186
                          Α1
                                20070502
                                            EP 2003-819324
                                                                   20030701
            AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IT, LI, LU, MC, NL, PT, RO, SE, SI, SK, TR
PRIORITY APPLN. INFO.:
                                            US 2002-393713P
                                                                Ρ
                                                                   20020703
                                            WO 2003-US20828
                                                                W
                                                                   20030701
    The invention discloses a method for producing large lots of final sterile
     poly-ICLC suitable for clin. use with reduced toxicity
     at ED levels, as well as a method for using poly-ICLC
     to regulate genes and a method for using poly-ICLC to
     treat certain human and veterinary infectious, neoplastic and autoimmune
     disorders.
     ANSWER 2 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:
                         1988:216000 CAPLUS
DOCUMENT NUMBER:
                         108:216000
                         Interferon induction in piglets with
TITLE:
                         polyinosinic:polycytidylic acid complexed with poly-L-
                         lysine and carboxymethylcellulose
AUTHOR (S):
                         Loewen, K. G.; Derbyshire, J. B.
CORPORATE SOURCE:
                         Dep. of Vet., Univ. Guelph, Guelph, N1G 2W1, Can.
                         Research in Veterinary Science (1988), 44(1), 132-3
SOURCE:
                         CODEN: RVTSA9; ISSN: 0034-5288
DOCUMENT TYPE:
                         Journal
LANGUAGE:
                         English
     When newborn piglets were inoculated i.v. with 1.0, 0.5 or 0.25 mg kg-1 of
     poly I:C complexed with poly-L-lysine and CM-cellulose (
     poly ICLC), the highest serum interferon levels and the
     lowest white blood cell counts were found in response to a dose of 0.5 mg
     kg-1. Similar responses were observed in weaned piglets inoculated with 0.25
     mg kg-1 of poly ICLC. Poly ICLC
     was a more effective interferon inducer than poly I:C, particularly in
     newborn piglets.
     ANSWER 3 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
L3
ACCESSION NUMBER:
                         1988:142978 CAPLUS
DOCUMENT NUMBER:
                         108:142978
TITLE:
                         Increase in liver-associated natural killer activity
                         by polyribonucleotides
AUTHOR (S):
                         Twilley, Theresa A.; Mason, Lewellyn; Talmadge, James
                         E.; Wiltrout, Robert H.
CORPORATE SOURCE:
                         Lab. Exp. Immunol., Biol. Response Modifiers Program,
                         Frederick, MD, USA
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Natural Immunity and Cell Growth Regulation (1987),

DOCUMENT TYPE: Journal LANGUAGE: English

6(6), 279-90

CODEN: NICRDR; ISSN: 0254-7600

SOURCE:

In mice, polyinosinic-polycytidylic acid and poly-L-lysine which AB has been stabilized in carboxymethylcellulose (polyICLC) as well as polyadenosinic-polyuridylic acid (poly AU), both potently augmented natural killer (NK) activity in the liver. Following the administration of poly ICLC (10 μ g/mouse) greater NK activity, as measured by lytic units (LU), was observed in the liver (445 LU) than in blood (63 LU) or spleen (20 LU). The high level of NK activity in the liver was in contrast to the low levels observed in untreated mice, and was maintained for at least 9 days post injection. NK activity in the blood and spleen returned to normal levels by day 6. Similar results were obtained with polyAU except that approx. 10-fold more poly AU (100 µg/mouse) was required to induce optimal augmentation of NK activity. The increase in liver-associated NK activity induced by poly ICLC was associated with a 10- to 20-fold increase in liver-associated leukocytes, termed nonparenchymal cells (NPC). The NK activity mediated by NPC was associated with cells morphol. characterized as large granular lymphocytes (LGL). The repeated administration of poly ICLC resulted in higher levels of liver-associated NK activity and total liver-associated LGL as compared to a single injection.

ANSWER 4 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1988:15951 CAPLUS

DOCUMENT NUMBER: 108:15951

TITLE: Toxicity of polyinosinic-polycytidylic acid admixed

with poly-L-lysine and solubilized with

carboxymethylcellulose in mice

AUTHOR (S): Hartmann, Diethelm; Schneider, Mark A.; Lenz, Barbara

F.; Talmadge, James E.

CORPORATE SOURCE: Preclin. Screening Lab., Natl. Cancer Inst.,

Frederick, MD, USA

SOURCE: Pathology and Immunopathology Research (1987), 6(1),

37-50

CODEN: PIREEI; ISSN: 0257-2761

DOCUMENT TYPE: Journal LANGUAGE: English

Polyinosinic-polycytidylic acid admixed with poly-L-lysine and solubilized with carboxymethylcellulose (poly(I,C)-LC) reduced the body wts. of treated mice and induced hepatic necrosis and pulmonary toxicity after i.p. and i.v. administrations, resp. The body wts. recovered with time despite repeated treatments.

ANSWER 5 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1986:205212 CAPLUS

DOCUMENT NUMBER: 104:205212

TITLE:

Potentiation of the cytocidal effect of human immune

interferon by different synthetic double-stranded RNAs in the refractory human colon carcinoma cell line BE

AUTHOR (S): Chapekar, Mrunal S.; Glazer, Robert I.

CORPORATE SOURCE: Lab. Biol. Chem., Natl. Cancer Inst., Bethesda, MD,

20892, USA

SOURCE: Cancer Research (1986), 46(4, Pt. 1), 1698-702

CODEN: CNREA8; ISSN: 0008-5472

DOCUMENT TYPE: Journal

LANGUAGE: English

A human cell line BE, derived from an undifferentiated carcinoma of the colon, was studied for its response to the cytocidal effects of human immune interferon (IFN- γ) alone and in combination with various double-stranded RNAs (dsRNAs). BE cells were moderately refractory to 3-day treatment with IFN- γ (10-300 units/mL) where only 5-30% reduction in colony formation occurred. A similar exposure interval to poly(I) poly(C) (100 μg/mL) had no detectable effect on colony formation. In contrast, the lethal effect of the combination of IFN- γ and poly(I) poly(C) was synergistic and this regimen produced a 40-80% reduction in colony formation. The cytocidal effects of the combination of IFN- γ with varying concns. of the dsRNAs

poly(I) poly(C), poly(A) poly(U), polyinosinic polyribocytidylic acid stabilized with poly -L-lysine in carboxymethylcellulose [poly(ICLC)], and mismatched dsRNA [rIn·r(C13,U)n] were also examined The concentration of the dsRNAs producing a 50% decrease in cell viability in combination with IFN- γ (100 units/mL) was 6 μ g/mL for poly(I) poly(C), 1 μ g/mL for poly(A) poly(U), 3 ng/mL for poly(ICLC), and 16 μ g/mL for rIn·r(C13,U)n. DNA, RNA, and protein synthesis in IFN- γ and poly(I) poly(C)-treated cells were reduced in a dose-dependent manner. There were no changes in either (2',5')oligoadenylate concns. or in rRNA transcription following treatment with IFN- γ and poly(I) poly(C). Thus, the synergism resulting from the combination of IFN- γ and dsRNA appears to be mediated via another, as yet unknown, mechanism.

L3 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

CORPORATE SOURCE:

1986:14714 CAPLUS

DOCUMENT NUMBER:

104:14714

TITLE:

Purification of carboxymethylcellulose decreases toxicity of poly ICLC in

mice

AUTHOR(S):

Bello, Jake; O'Malley, Judith; Granados, Edward Dep. Biophys., Roswell Park Mem. Inst., Buffalo, NY,

14263, USA

SOURCE:

AB

Journal of Interferon Research (1985), 5(3), 429-30

CODEN: JIREDJ; ISSN: 0197-8357

DOCUMENT TYPE:

Journal English

LANGUAGE:

Purification of the carboxymethylcellulose (CMC) component of polyinosinic polycytidylic acid poly-L-lysine carboxymethylcellulose (I) [59789-29-6] by EtOH extraction did not

significantly affect the efficacy of I as an interferon inducer in mice, but decreased the toxic side effects.

L3 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1986:14713 CAPLUS

DOCUMENT NUMBER:

104:14713

TITLE:

A comparison of interferon responses to poly

ICLC in males and females

AUTHOR(S):

Bever, Christopher T., Jr.; McFarlin, Dale E.; Levy,

Hilton B.

CORPORATE SOURCE: SOURCE:

Neuroimmunol. Branch, NINCDS, Bethesda, MD, USA Journal of Interferon Research (1985), 5(3), 423-8

CODEN: JIREDJ; ISSN: 0197-8357

DOCUMENT TYPE:

Journal English

LANGUAGE: Engl

AB Interferon (IFN) responses to polyriboinosinic acid polyribocytidylic acid polyr-L-lysine ·

carboxymethylcellulose (poly ICLC)

[59789-29-6] were studied in humans as part of a preliminary trial in patients with multiple sclerosis (MS). Patients received i.v. doses of 100 $\mu g/kg$ poly ICLC. Men and women produced substantial levels of IFN at 8, 12, and 16 h after infusion, but the levels of IFN in men were consistently higher. Interferon responses were also examined in male and female Rhesus monkeys. Again, there were higher levels of IFN in males. The observed differences may reflect sex-linked differences in either drug metabolism or specific sensitivity to IFN induction by poly ICLC. The most interesting possibility is that the difference is due to a more general difference in IFN response between males and females.

L3 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1985:605785 CAPLUS

DOCUMENT NUMBER:

103:205785

TITLE: Response of mouse tumor to interferon inducer and

radiation

Lvovsky, Edward A.; Mossman, Kenneth L.; Levy, Hilton AUTHOR (S):

B.; Dritschilo, Anatoly

CORPORATE SOURCE: Med. Cent., Georgetown Univ., Washington, DC, 20007,

SOURCE: International Journal of Radiation Oncology, Biology,

> Physics (1985), 11(9), 1721-5 CODEN: IOBPD3; ISSN: 0360-3016

DOCUMENT TYPE: Journal

LANGUAGE: English

The antitumor effect of interferon inducer poly(ICLC) (polyriboinosinic acid-polyribocytidylic acid-poly-Llysine-carboxymethylcellulose complex) [59789-29-6],

given prior to radiation treatment of Lewis lung carcinoma in C57B1 mice was studied. The local response, as measured by the delay in the tumor growth, was significantly higher in the combination treatment group than in poly(ICLC) or local irradiation groups. Following the termination of treatment, tumor regrowth was observed. The survival of poly(ICLC) treated mice was influenced by the number of transplanted tumor cells. Thus, untreated mice which received 3 + 104 or 3 + 105 (2 or 20 TD50) of tumor cells had similar mean survival time of 25.4 and 22 days, resp. The mice, treated by a combination of poly(ICLC) and local irradiation survived 48.2 days and 30.7 days, with higher survival in 2 TD50 tumor cell groups. Thus, data obtained in this study in mice showed that administration of an interferon inducer polyn(ICLC) prior to local irradiation can improve survival.

ANSWER 9 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1985:469574 CAPLUS

DOCUMENT NUMBER: 103:69574

TITLE: The in vitro induction of colony-stimulating factor,

prostaglandin E, and interferon in macrophages and

tumor cells by biological response modifiers Schlick, Erich; Hartung, Klaus; Piccoli, Mario;

Bartocci, Anna; Chirigos, Michael A.

Frederick Cancer Res. Facil., Natl. Cancer Inst., CORPORATE SOURCE:

Frederick, MD, USA

SOURCE: Immunology Series (1984), 25(Immune Modulation Agents

Their Mech.), 513-29

CODEN: IMSED7; ISSN: 0092-6019

DOCUMENT TYPE: Journal LANGUAGE: English

The effects of 6 biol. response modifiers (BRMs) on the secretion of colony-stimulating factors (CSFs), prostaglandin E, and interferon were studied using resident peritoneal macrophages (MO) and 2 tumor cell lines, Wehi-3 and L1210, in an in vitro system. The BRMs most effective for M0 were lipopolysaccharide (LPS), interferon (IF), and polyriboinosinic acid-polycytidylic acid poly-L-lysine stabilized with

carboxymethylcellulose (poly ICLC). However,

only poly ICLC induced considerable amts. of IF in MO.

The same 3 BRMs induced CFS production by the 2 tumor cell lines whereas none of the drugs could induce prostaglandin E and only poly

ICLC stimulated marginal IF titers (.apprx.10 units/mL) in the

cell lines.

AUTHOR (S):

ANSWER 10 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN L3

ACCESSION NUMBER: 1985:464451 CAPLUS

DOCUMENT NUMBER: 103:64451

TITLE: Cellular regulation by immunomodifiers MVE-2 and

poly ICLC and their therapeutic

application

AUTHOR (S): Chirigos, Michael A.; Saito, Tohru; Schlick, Erich;

Ruffman, Ralf

CORPORATE SOURCE: Frederick Cancer Res. Fac., Natl. Cancer Inst.,

Frederick, MD, 21701, USA

SOURCE: NIH Publ. (1985), n85-1177, Cancer Treat. Symp., 1985,

> Vol. 1, 11-18 CODEN: DPNSDO

DOCUMENT TYPE:

Report English

LANGUAGE: Two immunomodifiers, maleic anhydride divinyl ether copolymer (MVE-2)

[27100-68-1] and polyinosinic-polycytidylic acid poly-L-lysine

stabilized with carboxymethylcellulose (poly [59789-29-6], augmented natural killer (NK) cell activity in several tissues. Macrophage tumoricidal activity was also markedly increased. Both effector cells were active for 1 wk, with macrophage activity remaining elevated for a longer period. Multiple treatment with both agents resulted in a decrease in NK cell response, but macrophage activity remained elevated; NK cells had the greatest hyporesponsiveness to MVE-2. Both agents caused an increase in secretion of colony-stimulating factor from bone marrow cells and in serum. Treatment with MVE-2 and poly ICLC resulted in an earlier reconstitution of bone marrow cells, NK cell activity, and macrophage effector cell activity in mice pretreated with cyclophosphamide [50-18-0]; MVE-2 prevented the establishment of B16 melanoma metastasis in

lung and liver. Thus, NK cells and macrophages play a supportive role in the natural resistance to tumor cell replication. Combined treatment of MBL-2 tumor cells with cytoreductive chemotherapy with cyclophosphamide and MVE-2 resulted in an enhanced therapeutic response.

ANSWER 11 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1985:432069 CAPLUS

DOCUMENT NUMBER: 103:32069

TITLE: Poly ICL-CM dextran: an interferon inducer of reduced

toxicity

Granados, Edward N.; Dawidzik, Jean; O'Malley, Judith; AUTHOR (S):

McGarry, Michael; Bello, Jake

Abbott Lab., North Chicago, IL, 60064, USA CORPORATE SOURCE:

SOURCE: Journal of Interferon Research (1984), 4(2), 155-60

CODEN: JIREDJ; ISSN: 0197-8357

DOCUMENT TYPE: Journal LANGUAGE: English

AB Poly ICL-CM dextran [97127-12-3] (a complex of polyinosinate polycytidylate, poly-L-lysine, and

carboxymethyldextran) was as effective an inducer of interferon in mice and rhesus monkeys as poly ICLC (the counterpart of

poly ICL-CM dextran which contains carboxymethylcellulose instead of carboxymethyldextran). In addition, poly ICL-CM dextran showed lower toxicity in mice than poly ICLC.

ANSWER 12 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1983:137376 CAPLUS

DOCUMENT NUMBER: 98:137376

TITLE: Inhibition of virus-induced murine diabetes by an

interferon inducer

AUTHOR (S): Gadzik, James P.; Naji, Ali; Barker, Clyde F.; Blank,

Kenneth J.

CORPORATE SOURCE: Sch. Med., Univ. Pennsylvania, PA, USA

SOURCE: Journal of Interferon Research (1982), 2(1), 59-63

CODEN: JIREDJ; ISSN: 0197-8357

DOCUMENT TYPE: Journal LANGUAGE: English

Administration of the interferon inducer poly (I) ·poly(C) -poly-Llysine in carboxymethylcellulose (I) prior to inoculation with the picornavirus, encephalomyocarditis virus (EMCV), and at 48 and 96 h thereafter effectively blocked the induction of diabetes in mice during a 36-day period. Pretreatment with a single dose of I prior to virus inoculation afforded protection during the 1st wk after infection (as indicated by a decreased hyperglycemia), but was a transient effect.

L3 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1982:504227 CAPLUS

DOCUMENT NUMBER:

97:104227

TITLE:

Poly(ICL) as an effective interferon inducer

INVENTOR(S):

Levy, Hilton B.; Riley, Freddie L.

PATENT ASSIGNEE(S):

United States Dept. of Health and Human Services, USA

APPLICATION NO.

DATE

SOURCE:

U. S. Pat. Appl., 24 pp. Avail. NTIS Order No.

PAT-APPL-6-292 583.

DATE

CODEN: XAXXAV

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

KIND

PATENT NO.

PATENT INFORMATION:

	US 292583	A0	19820618	US 1981-292583	19810831
PRIORITY APPLN. INFO.:			US 1981-292583	19810831	
AB A polyriboinosinic-polyribocytidylic-poly-L-lysine complex					
	<pre>[poly(ICL)] [35560-71-5] containing different amts. of poly-L-lysine [poly(L)] was prepared by dropwise addition at 58-60° of different vols. of a poly(L) solution to a solution which had been prepared from equal amts. of polyriboinosinic [poly(I)] and polyribocytidylic [poly(C)] stock solns. The poly(ICL) complexes were as effective interferon inducers in mice as was a previously described poly(I:C)-poly(L)-</pre>				
	carboxymethylcellulose [poly(ICLC)] complex,				
	and more effective than poly(I:C). Poly(ICL) was less toxic in mice than was poly(ICLC) (i.p. LD50 values of 25.1 and 12.6 mg/kg, resp.). The poly(ICL) complex with the highest amount of poly(L) induced the highest levels of interferon in Rhesus monkeys. Advantages of the poly(ICL) complex over the poly(
	ICLC) complex are	discusse	ed.		

ANSWER 14 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

CORPORATE SOURCE:

1982:503984 CAPLUS

DOCUMENT NUMBER:

97:103984

TITLE:

Interferon induction and therapy of brain tumors in

rats by poly(ICLC)

AUTHOR (S):

Machida, Haruhiko; Takezawa, Junichi; Kuninaka, Akira; Yoshino, Hiroshi; Nakamura, Osamu; Takakura, Kintomo Res. Lab., Yamasa Shoyu Co. Ltd., Choshi, 288, Japan

SOURCE:

Microbiology and Immunology (1982), 26(4), 353-8

CODEN: MIIMDV; ISSN: 0385-5600

DOCUMENT TYPE:

Journal

LANGUAGE: English

The levels of plasma interferon in rats 4 h after injection of several doses (0.05-5 mg/kg) of poly(ICLC)-B or -C [poly(I) poly(C) stabilized with varying amts. of poly-Llysine-carboxymethylcellulose [59789-29-6]] were the same as those in rats receiving equal doses of poly(I) poly(C) [24939-03-5]. (The amount of inducer is expressed in terms of poly(I) poly(C) content of each preparation. However, the interferon level of plasma persisted for a longer time, in rats injected with poly(ICCL)-B than in those injected with just poly(I) poly(C). Treatment with poly(ICLC)-B (i.v.) was moderately effective in increasing the survival time of rats inoculated intracerebrally with glial tumor cells when the treatment was started by 7 days after tumor cell inoculation. Thus, the antitumor activity of poly(ICLC)-B is correlated with persistence of the high level of interferon induced thereby, and, probably also with the immune adjuvant activity of poly(ICLC).

ACCESSION NUMBER:

1982:135517 CAPLUS

DOCUMENT NUMBER:

96:135517

TITLE:

Polyriboinosinic-polyribocytidylic acid-poly-L-

lysine complex [poly(ICL)] without carboxymethylcellulose (CMC): primate-effective interferon inducer

AUTHOR(S):

Riley, Freddie L.; Morin, Martin L.; Lvovsky, Eduard;

Stephens, Edward E.; Levy, Hilton B.

CORPORATE SOURCE:

Natl. Inst. Allergy Infect. Dis., Bethesda, MD, 21701,

USA

SOURCE:

Proceedings of the Society for Experimental Biology

and Medicine (1982), 169(2), 183-8

CODEN: PSEBAA; ISSN: 0037-9727

DOCUMENT TYPE:

Journal

LANGUAGE:

English

The complex of poly(I).poly(C) with poly-(L-lysine) in 0.5% carboxymethylcellulose (CMC) [poly(ICLC)] has

proven to be an effective interferon inducer in primates, including man. Since no mechanism is known by which the body can degrade CMC, a new complex of lower mol. weight, which contains poly I.poly C complexed with poly-L-lysine [poly(ICL)], but without CMC, was developed. This

compound is slightly more resistant than poly(ICLC) to

hydrolysis by RNase A and is also an effective inducer of interferon in nonhuman primates. The new compound without CMC is also less toxic in mice than is poly(ICLC) as indicated by LD50 values.

ANSWER 16 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1982:83980 CAPLUS

DOCUMENT NUMBER:

96:83980

TITLE:

Immune response modifying activity in mice of polyinosinic: polycytidylic acid stabilized with

poly-L-lysine, in

carboxymethylcellulose [poly-

· ICLC]

AUTHOR (S):

Chirigos, M. A.; Papademetriou, V.; Bartocci, A.;

Read, E.; Levy, H. B.

CORPORATE SOURCE:

Div. Cancer Treat., Natl. Cancer Inst., Bethesda, MD,

20205, USA

SOURCE:

International Journal of Immunopharmacology (1981),

3(4), 329-37

CODEN: IJIMDS; ISSN: 0192-0561

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB Poly-ICLC, a polyinosinic polycytidylic acid stabilized with poly-L-lysine in carboxymethyl-

cellulose, was tested in mice for its immunoregulatory activity.

Poly-ICLC enhanced T cell responsiveness but not B cell

responsiveness. It augmented the delayed type hypersensitivity response significantly. The results indicate that Poly-ICLC is

a T cell stimulator. Macrophage tumoricidal activity was markedly

enhanced both in vitro and in vivo after exposure to Poly-ICLC. Natural killer cell cytotoxicity was significantly

augmented in vivo. Both macrophage and natural killer cell activity was maintained for over 3 days after only one treatment. The extended period of tumor cell cytotoxicity, exhibited by macrophage and natural killer cells, may correlate to Poly-ICLC induction of early

and high levels of interferon which are maintained in the serum for a longer period of time.

ANSWER 17 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1980:597823 CAPLUS

DOCUMENT NUMBER:

93:197823

TITLE:

Modified polyriboinosinic-polyribocytidylic acid complex: modulation of toxicity for rabbits by alterations in components

AUTHOR(S): Gatmaitan, Bienvenido G.; Levy, Hilton B.; Lerner, A.

Martin

CORPORATE SOURCE:

VA Med. Cent., Allen Park, MI, 48101, USA

SOURCE:

Antimicrobial Agents and Chemotherapy (1980), 18(3),

CODEN: AMACCQ; ISSN: 0066-4804

DOCUMENT TYPE:

Journal English

LANGUAGE: The effects of a modified complex of polyriboinosinic acidpolyribocytidylic acid [poly(I)-poly(C)] with

carboxymethylcellulose and poly-L-lysine [

[59789-29-6]], namely, the induction of high

titers of serum interferon along with fever and hypotension, were reproduced in rabbits. The effects of complexes with homopolymer polyribonucleotide sedimentation coeffs. decreasing from 9S to 6S and 4S were evaluated. Modified complexes of carboxymethylcellulose and poly-L-lysine with decreasing mol. wts. were also tested. In several studies diphenhydramine [58-73-1] and indomethacin [53-86-1] were administered concomitantly. At a daily i.v. dose of 0.2 mg/kg, the various prepns. of poly(I)-poly-(C) (9S) and poly(I)-poly(C) (6S) induced falls in blood pressure, but stabilized complexes of poly(I)-poly(C) (4S) did not. Alterations in the mol. wts. of carboxymethylcellulose

and poly-L-lysine in the modified complex and the concomitant administration of diphenhydramine did not influence the occurrence or severity of untoward reactions. In rabbits, poly(ICLC

) (4S) along with indomethacin induced high titers of serum interferon without fever or hypotension.

ANSWER 18 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1980:507229 CAPLUS

DOCUMENT NUMBER:

93:107229

TITLE:

Interferon induction by and toxicity of

polyriboinosinic acid [poly(rI)].polyribocytidylic

acid [poly(rC)], mismatched analog

poly(rI).poly[r(C12uracil)n], and poly(rI).poly(rC) L-

lysine complexed with carboxymethylcellulose

AUTHOR(S):

Stringfellow, Dale A.; Weed, Sheldon D.

CORPORATE SOURCE: SOURCE:

Exp. Biol. Res., Upjohn Co., Kalamazoo, MI, 49001, USA

Antimicrobial Agents and Chemotherapy (1980), 17(6),

988-92

CODEN: AMACCQ; ISSN: 0066-4804

DOCUMENT TYPE:

Journal

LANGUAGE: English

The ability of polyriboinosinic acid polyribocytidylic acid (poly AB

I.polyC) [24939-03-5], mismatched analog poly

I·poly[(C12Uracil)n] [38640-92-5], and poly I·poly C complexed with poly L-lysine and

carboxymethylcellulose [poly(ICLC)]

[59789-29-6] to induce interferon and the comparative toxicity of each in cats were evaluated. Each induced high levels of circulating interferon,

although poly(ICLC) injected i.v. at 1 to 4 mg/kg

induced ≤10-fold more interferon than the other compds. Each

compound was pyrogenic and caused a transient decrease in leukocyte nos.

Poly I polyC and the mismatched analog caused severe diarrhea and nausea at the highest drug concns. (1 to 4 mg/kg), but poly(ICLC) did not. Each compound also caused depression and letharqy

and impaired coordination.

ANSWER 19 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN L3

ACCESSION NUMBER:

1979:418239 CAPLUS

DOCUMENT NUMBER:

91:18239

TITLE:

Adjuvant effects of low doses of a nuclease-resistant derivative of polyinosinic acid.polycytidylic acid on

antibody responses of monkeys to inactivated

AUTHOR(S): Venezuelan equine encephalomyelitis virus vaccine Harrington, D. G.; Crabbs, C. L.; Hilmas, D. E.;

Brown, J. R.; Higbee, G. A.; Cole, F. E., Jr.; Levy,

н. в.

CORPORATE SOURCE: Army Med. Res. Inst. Infect. Dis., Fort Detrick,

Frederick, MD, 21701, USA

SOURCE: Infection and Immunity (1979), 24(1), 160-6

CODEN: INFIBR; ISSN: 0019-9567

DOCUMENT TYPE: Journal LANGUAGE: English

AB Polyriboinosinic polyribocytidylic acid [poly(I) poly(C)] stabilized with poly-1-lysine and CM-cellulose [poly(

ICLC)] has been previously shown to be a compound with marked

adjuvant activity when given in high doses with inactivated Venezuelan equine encephalomyelitis (VEE) virus vaccine. This study investigated the

effects of much lower doses of poly(ICLC) on the

magnitude and kinetics of the primary and secondary humoral antibody responses of rhesus monkeys to inactivated VEE virus vaccine. Monkeys given a single injection of vaccine developed very low neutralizing antibody titers, whereas those given adjuvant plus vaccine had

30-100-fold-higher titers which remained elevated for >6 mo. Low doses of

poly(ICLC) given with VEE virus vaccine resulted in a

profound but transient increase in priming of secondary antibody responses to the antigen. In contrast, the administration of poly-1-lysine and CM-cellulose alone without the poly(I)·poly(C) component of the complex had no adjuvant effect on antibody responses of monkeys to VEE

virus vaccine. The temporal development of antibody by class (IgM-IgG) in monkeys given 2 injections of adjuvant-vaccine was not different from that with vaccine alone. Serial hematol. and clin. chemical detns. on monkeys

given single or multiple doses of poly(ICLC) with

vaccine were not different from values in monkeys given vaccine alone.

L3 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1979:400321 CAPLUS

DOCUMENT NUMBER: 91:321

TITLE: Protective and toxic effects of a nuclease-resistant

derivative of polyriboinosinic-polyribocytidylic acid on Venezuelan equine encephalomyelitis virus in Rhesus

monkeys

AUTHOR(S): Stephen, E. L.; Hilmas, D. E.; Levy, H. B.; Spertzel,

R. O.

CORPORATE SOURCE: Army Med. Res. Inst. Infect. Dis., NIH, Bethesda, MD,

USA

SOURCE: Journal of Infectious Diseases (1979), 139(3), 267-72

CODEN: JIDIAQ; ISSN: 0022-1899

DOCUMENT TYPE: Journal LANGUAGE: English

AB Poly I-poly C [24939-03-5], stabilized with poly-L-

lysine and carboxymethylcellulose (poly

ICLC), favorably altered the pathogenesis of Venezuelan equine encephalomyelitis virus infection in rhesus monkeys by decreasing the number of infected monkeys that became detectably viremic and by delaying the onset of viremia in the remaining monkeys. The death of some infected, treated monkeys in the absence of death in monkeys that were either infected and untreated or treated and uninfected suggests a synergistic toxicity resulting from the combination of infection, handling, and poly ICLC treatment, although other explanations are possible.

L3 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1978:523224 CAPLUS

DOCUMENT NUMBER: 89:123224

TITLE: Effect of interferon on togavirus and arenavirus

infections of animals

AUTHOR(S): Stephen, E. L.; Scott, S. K.; Eddy, G. A.; Levy, H. B.

CORPORATE SOURCE: U. S. Army Med. Res. Inst. Infect. Dis., Fort Detrick,

MD, USA

SOURCE: Texas Reports on Biology and Medicine (1977),

35(Interferon Syst.), 449-54 CODEN: TRBMAV; ISSN: 0040-4675

DOCUMENT TYPE:

LANGUAGE:

Journal English

AB Machupo virus-infected monkeys treated early in infection with the

interferon inducer poly(ICLC) [poly

(I).cntdot.poly(C)-carboxymethylcellulose-poly-L-

lysine complex] had significantly higher viremias than did

untreated, control monkeys. A possible explanation for the higher

viremias is that interferon and/or poly(ICLC) either

altered or stimulated the production of certain cell types that are target tissues for viral replication. The results are discussed with respect to the sensitivity of togavaruses and arenaviruses to interferon.

L3 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1978:83623 CAPLUS .

DOCUMENT NUMBER:

88:83623

TITLE:

SOURCE:

Use of poly(ICLC) for the

prophylaxis and treatment of Venezuelan equine

encephalomyelitis virus infection in nonhuman primates

AUTHOR(S): Hilmas, Duane E.; Stephen, Edward L.; Spertzel,

Richard O.; Levy, Hilton B.

CORPORATE SOURCE:

Army Med. Res. Inst. Infect. Dis., Frederick, MD, USA

U. S. NTIS, AD Rep. (1977), AD-A044417, 13 pp.

Avail.: NTIS

From: Gov. Rep. Announce. Index (U. S.) 1977, 77(24),

92

CODEN: XADRCH; ISSN: 0099-8575

DOCUMENT TYPE:

Report English

LANGUAGE: English

AB Poly(I) · poly(C) stabilized with poly-L-lysine

and carboxymethylcellulose [poly(ICLC)]

[59789-29-6] induced moderate to high levels of serum interferon in man, nonhuman primates, and rodents. Poly(ICLC) was tested therapeutically in rhesus monkeys against infection with a virulent strain of Venezuelan equine encephalomyelitis (VEE) virus. The VEE-1 strain of virus in exptl. infections presents a broad spectrum of interactions with different hosts, ranging from mild, subclin. infections to severe, prostrating disease and death. In monkeys, clin. signs of exptl. infection are generally of a mild form, with a characteristic biphasic febrile response clearly detectable but nonlethal. This strain of virus is sensitive to interferon in vitro. Several monkeys inoculated with 1000 plaque-forming units or more of VEE-1 virus died (11-20 days) subsequent to infection when treated with 3.0 mg/kg of poly(ICLC

). Poly(ICLC) is reported to be an effective

antiviral agent against lethal yellow fever and Japanese encephalitis virus infections in monkeys. The variable response found following treatment of VEE virus disease in monkeys suggests caution regarding the indiscriminate use of poly(ICLC) to treat virus infections that have not been specifically evaluated with respect to their

infections that have not been specifically evaluated with respect to their response to this drug.

L3 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1978:292 CAPLUS

DOCUMENT NUMBER:

88:292

TITLE:

Effect of a nuclease-resistant derivative of polyriboinosinic-polyribocytidylic acid complex on

yellow fever in rhesus monkeys (Macaca mulatta)

AUTHOR(S): Stephen, E. L.; Sammons, M. L.; Panni

Stephen, E. L.; Sammons, M. L.; Pannier, W. L.; Baron,

S.; Spertzel, R. O.; Levy, H. B.

CORPORATE SOURCE:

U. S. Army Med. Res. Inst. Infect. Dis., Fort Detrick,

Frederick, MD, USA

Journal of Infectious Diseases (1977), 136(1), 122-6 SOURCE:

CODEN: JIDIAQ; ISSN: 0022-1899

DOCUMENT TYPE:

LANGUAGE: English

Rhesus monkeys (Macaca mulatta) treated with a newly developed nuclease-resistant polyriboinosinic-polyribocytidylic acid-poly

-L-lysine-carboxymethylcellulose complex [poly

Journal

[64685-78-5] did not die after challenge with virulent

Asibi strain yellow fever (YF) virus. The strain of virus is sensitive to the effects of interferon in vitro and is lethal for rhesus monkeys 4 to 6 days after s.c. administration of 1,000 plaque-forming units of the virus. The mortality rate was reduced in monkeys initially treated 8 h before or after inoculation of virus but was unchanged in monkeys initially treated 24 h after challenge. Treated monkeys developed neutralizing antibody to YF virus. The successful treatment of yellow fever in a primate model with use of poly (ICLC) suggests a meaningful role for

the interferon system in the host defense against this viral infection.

ANSWER 24 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

1977:565851 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 87:165851

TITLE: Swine influenza virus vaccine: potentiation of

antibody responses in rhesus monkeys

AUTHOR (S): Stephen, E. L.; Hilmas, D. E.; Mangiafico, J. A.;

Levy, H. B.

CORPORATE SOURCE: U. S. Army Med. Res. Inst. Infect. Dis., Frederick,

MD, USA

SOURCE: Science (Washington, DC, United States) (1977),

197 (4310), 1289-90

CODEN: SCIEAS; ISSN: 0036-8075

DOCUMENT TYPE: Journal LANGUAGE: English

Polyriboinosinic-polyribocytidylic acid stabilized with poly-L-

lysine and carboxymethylcellulose [poly(

ICLC)] enhances the antibody response in rhesus monkeys immunized with swine influenza virus subunit vaccine. Monkeys given the vaccine-adjuvant combination had earlier and higher titers by 14 days compared to those that received vaccine alone. The potentiation of the antibody response of young monkeys given a split-virus vaccine in combination with poly(ICLC) suggests that this

vaccine-adjuvant combination may similarly provide a potentially useful alternative approach to the immunization of pediatric and young adult age groups against swine influenza.

ANSWER 25 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1977:69998 CAPLUS

DOCUMENT NUMBER: 86:69998

AUTHOR (S):

TITLE: Interferon induction in cynomolgus and rhesus monkeys

after repeated doses of a modified

polyriboinosinic-polyribocytidylic acid complex Sammons, M. L.; Stephen, E. L.; Levy, H. B.; Baron,

S.; Hilmas, D. E.

CORPORATE SOURCE: U. S. Army Med. Res. Inst. Infect. Dis., Fort Detrick,

Frederick, MD, USA

SOURCE: Antimicrobial Agents and Chemotherapy (1977), 11(1),

80-3

CODEN: AMACCQ; ISSN: 0066-4804

DOCUMENT TYPE: Journal LANGUAGE: English

Serum interferon activity was determined in 12 cynomolgus and 12 rhesus monkeys injected i.v. once daily for 10 days with 0.1-6.0 mg/kg of a stabilized

poly(riboinosinic acid) poly(ribocytidylic acid)complex, composed

of poly(riboinosinic acid) poly(ribocytidylic acid), poly

-L-lysine, and carboxymethylcellulose [poly(

ICLC]. Interferon activity was detected 2 h after the first

injection, with maximum activity occurring 8 h after the second injection. A period of hyporesponsiveness occurred after the third injection of poly(ICLC) in all monkeys and lasted until the sixth injection in the rhesus monkeys, when interferon activity again became more elevated. The delayed rebound was not as apparent in cynomolgus monkeys. Rhesus monkeys injected with 6 mg/kg did not exhibit serious side effects.

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L1 94 S (POLY (5A) ICLC)

L2 2 L1 AND PREP/RL

E LYSINE+ALL/CT

E CARBOXYMETHYLCELLULOSE+ALL/CT

L3 25 S L1 AND LYSINE AND (CARBOXYMETHYLCELLULOSE OR "CARBOXYMETHYL C

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